Applicant gratefully acknowledges that all previous rejections under 35 U.S.C. §112, first paragraph, were found to have been overcome, and that Claims 8-11, 13-16, and 19-31 were found to contain allowable subject matter.

Amendments to the Claims

Claim 16 was amended to place this claim in independent form, including the limitations of intervening claims 2-5. Thus, the objections to this claim and claims 19-31, which depend thereon, have been removed.

Claim 1 has been amended with regard to the selections for the substituent R^3. The selection of heteroalkylamino was added in claim 1, line (t), to provide antecedent basis for this selection in claim 2, line (d) (note claims 16 and 22 which had recited heteroalkylamino were found to contain allowable subject matter). In line (q), applicant has recited that the alkylene group and groups R^{30} and R^{31} optionally may be substituted with one to two groups selected from OH and O(alkyl), as exemplified at pages and 57 and 72 of the specification. In line (r), applicant has recited the group CO_2NHR', which is exemplified at page 59 (Example 16) of the specification. In claim 2, line (n), applicant has recited that the alkylene group and groups R^{30} and R^{31} optionally may be substituted with one to two groups selected from OH and O(alkyl), as shown at pages and 57 and 72 of the specification. This recitation for the Z-alkylene-$NR^{30}R^{31}$ and Z-alkylene-OR^{32} groups is also included in claim 16.

The amendments to claims 1 and 2 do not comprise new matter as they are supported by the Examples herein (page numbers are recited above). Applicant further notes that the groups added to claims 1 and 2 are not found in the Faraci reference, WO 94/13643 ("Faraci").

New Claim 33

Applicant has added new Claim 33 which defines the substituent R^3 with provisos directed to the groups identified in the Office Action as allegedly creating overlap with Faraci. The proviso's do not constitute new matter. *See In re Johnson*, 194 USPQ 187, 196 (C.C.P.A. 1977).[1]

Response to Rejection under 35 U.S.C. §103(a)

Claims 1-7, 12, and 32 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Faraci, WO 94/13643 ("Faraci").

Applicant understands that the 103(a) rejection is based on the rationale that certain selections for R^3 in claim 1 overlap with selections for the substituents on the ring R^3 in Faraci. To the extent there is overlap in the selections, the Office Action concludes that the instant application recites a subgenus which is considered obvious in view of a larger genus in Faraci, arguing that the "selection of 'some' from 'many' is *prima facie* obvious." (Office Action at page 3). Applicant has submitted new claim 33 which excises from the definition of R^3 the groups that allegedly create an overlap, and thus, the argument in the Office Action does not apply to claim 33. Claim 33 is submitted, however, without prejudice to applicant's

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[1] In *In re Johnson, supra*, the appellant had inserted two provisos into claim 1 of his application to carve out from the generic claim two particular species that were lost in an interference. *See* 194 USPQ at 191. Chief Judge Markey of the Court of Customs and Patent Appeals (predecessor court to the Federal Circuit), held that the provisos did not constitute "new matter":

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach to those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of § 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. ....[A]ppellants are merely excising the invention of another, to which they are not entitled, and are not creating an "artificial subgenus" or claiming "new matter." [*Id.* at 196].

contention that the compounds defined by claim 1 do not overlap with Faraci and are not obvious in view of Faraci for the following reasons.

First, regarding the issue of overlap, each of the compounds identified in the Office Action (page 36, line 10, page 40, line 15, page 43, line 19, and page 44, lines 12-14), has a 3-methylthio group and a 1-phenyl substituent in turn having three substituents in the 2,4, and 6 positions. In the instant application, methylthio is not an optional 3-position substituent, and the 1-phenyl group has up to two substituents (R^5 and R^6). Thus, if one considers the Faraci compounds as a whole, and does not improperly dissect those compounds into discrete elements, there is no overlap. *See* MPEP 2141 ("The references must be considered as a whole") (*citing Hodosh v. Block Drug Co.*, 786 F.2d 1136, 1143 n. 5, 229 USPQ 182, 187 n. 5 (Fed. Cir. 1986)), and MPEP 2144.08 (the "invention may not be dissected into discrete elements to be analyzed in isolation but must be considered as a whole") (citing cases).

Second, there is no legal rule that the selection of "some" from "many" is *prima facie* obvious. Use of such *per se* rules is improper for determining obviousness. Moreover, "[t]he fact that a claimed species *or subgenus* is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness." MPEP § 2144.08 (II), citing *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

In determining obviousness in the case of a genus/subgenus, a first step is to determine the scope and content of the prior art *as a whole*, including such factors as the size of the prior art genus, the structure of the disclosed species, the physical properties of the compounds, and the number of species that fall within the genus. *See* MPEP § 2144.08 (II) (a)(1). Then, considering the size of the prior art genus, an analysis should be made whether one skilled in the field would have been motivated to select the claimed subgenus, given, for example, express teachings in the prior art and what is suggested for typical preferred compounds.

Looking at Faraci as a whole, a broad genus is described which includes an untold number of pyrazole-based compounds having two rings bonded or fused thereto (*see, e.g.*, page 14). The number of species encompassed by Faraci is difficult to quantify. The compounds are claimed to have CRF antagonist activity, rendering them effective primarily in treating stress-

related diseases, such as depression, anxiety and headache. (Faraci, page 1, lines 15-17, and page 4, lines 18-30). Particularly preferred species are identified in Faraci where R_2 is methylthio, R_3 is 2-chlorophenyl, and R_4 is 2,4,6-trichlorophenyl.

Thus, considering Faraci as a whole, it discloses a large genus of pyrazole-based compounds having CRF antagonist activity, and preferred selections are identified as having a 3-methylthio group, a 4-position phenyl in turn substituted at the 2-position (more preferably with Cl), and a 1-position phenyl having three small group substituents, such as Cl, Br, CF_3, CH_3, OCH_3, and the like. (*See* generally Faraci at pp. 31-47). One skilled in the field looking at Faraci would not have been motivated to identify a different genus of compounds having p38 kinase activity where the group R_2 is not methylthio, where the 1-position phenyl has two optional substituents, and where the 4-aryloxy group has a mandatory R_3 substituent as defined herein. While there is a general reference in Faraci to inflammatory conditions, the compounds in Faraci are designed to target CRF. One skilled in the field would not predict that a different, subgenus of pyrazole-based compounds, having different selections for the various substituents thereon, would have activity in inhibiting p38 kinase.

Accordingly, applicant requests that all rejections under 35 U.S.C. § 103(a) be withdrawn.

FEES

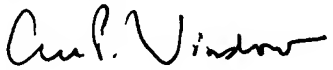
No fees should be due. One new claim was added, and claim 16 was placed in independent form. However, the case contains less than three independent claims and more than one claim was previously canceled. However, in the event it is determined that a fee is due, please charge same to Deposit Account No. 18-1700.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

The Examiner is invited to contact the undersigned by telephone at 650-852-1141 to expedite prosecution of this application. For the Examiner's convenience, a full set of the claims as pending should the instant amendments be entered is attached as Appendix B.

Respectfully submitted,



Anastasia P. Winslow
Reg. No. 40,875

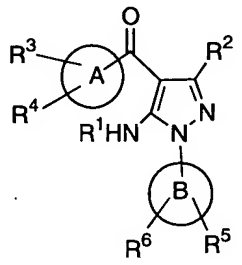
Roche Palo Alto LLC
Patent Law Dept. M/S A2-250
3401 Hillview Avenue
Palo Alto, CA 94304

Direct Phone: (650) 852-1141
Date: January 24, 2003

APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1, 2 and 16 have been amended as follows.

1. (Twice Amended) A compound selected from the group of compounds represented by Formula (I):



(I)

wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A and B are simultaneously an aryl or a heteroaryl ring;

R^3 is selected from the group consisting of:

(a) optionally substituted heterocyclyl;

(b) optionally substituted aryl or heteroaryl;

(c) heteroalkenyl;

(f) heteroalkynyl;

(e) optionally substituted heterocyclylalkyl;

(f) optionally substituted heterocyclylalkenyl;

(g) optionally substituted heterocyclylalkynyl;

(h) optionally substituted heterocyclylalkoxy, cyclyloxy or heterocyclyloxy;

(i) optionally substituted heterocyclylalkylamino;

(j) optionally substituted heterocyclylalkylcarbonyl;

(k) -Y-(alkylene)-R^9 where:

Y is a single bond, -O-, -NH- or -$S(O)_n$- (where n is an integer from 0 to 2); and

R^9 is cyano, optionally substituted heteroaryl, -COOH, -COR^{10}, -$COOR^{11}$, -$CONR^{12}R^{13}$, -SO_2R^{14}, -$SO_2NR^{15}R^{16}$, -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$, where R^{10} is optionally substituted heterocycle, R^{11} is alkyl, and R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(l) -$C(=NR^{20})(NR^{21}R^{22})$ where R^{20}, R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are -$(CH_2)_n$- where n is 2 or 3 and R^{22} is hydrogen or alkyl;

(m) -$NHC(X)NR^{23}R^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(n) -$CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

(o) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(p) arylaminoalkylene or heteroarylaminoalkylene;

(q) Z-alkylene-$NR^{30}R^{31}$ or Z-alkylene-OR^{32} where Z is -O-, and R^{30}, $R^{31}$and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl, wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl);

(r) -OC(O)-alkylene-CO_2H, ~~or~~ -OC(O)-NR'R" , or CO_2NHR' (where R' and R" are independently hydrogen or alkyl); ~~and~~

(u) heteroarylalkenylene or heteroarylalkynylene; and

(v) heteroalkylamino;

R^4 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) alkoxy; and

(e) hydroxy;

R^5 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) haloalkyl;

(e) thioalkyl;

(f) hydroxy;

(g) amino;

(h) alkylamino;

(i) dialkylamino;

(j) heteroalkyl;

(k) optionally substituted heterocycle;

(l) optionally substituted heterocyclylalkyl;

(m) optionally substituted heterocyclylalkoxy;

(n) alkylsulfonyl;

(o) aminosulfonyl, mono-alkylaminosulfonyl or di-alkylaminosulfonyl;

(p) heteroalkoxy; and

(q) carboxy;

R^6 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl; and

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

2. (Twice Amended) The compound of Claim 1 wherein R^3 is:

(a) optionally substituted heterocyclyl;

(b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO_2R' (where R' is alkyl) or $SO_2NHR'R''$ (where R' and R" are independently hydrogen or alkyl);

(c) heteroalkenyl;

(d) heteroalkylamino;

(e) optionally substituted heterocyclylalkyl or heterocyclyloxy;

(f) optionally substituted heterocyclylalkenyl;

(g) optionally substituted heterocyclylalkynyl;

(h) optionally substituted heterocyclylalkoxy;

(i) optionally substituted heterocyclylalkylamino;

(j) optionally substituted heterocyclylalkylcarbonyl;

(m) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, $-CONR^{12}R^{13}$, SO_2R^{14}, $-SO_2NR^{15}R^{16}$ - $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl,

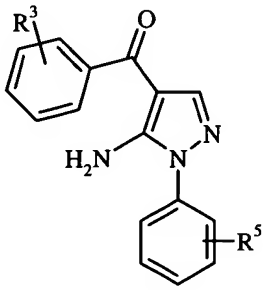
(n) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(m) arylaminoalkylene or heteroarylaminoalkylene; or

(n) Z-alkylene-$NR^{30}R^{31}$ where Z is -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl, <u>wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl).</u>

16. (Twice Amended) ~~The compound of Claim 5, wherein~~

A compound selected from the group of compounds represented by the Formula:



wherein:

R^5 is halo or alkyl; and

R^3 is:

(a) heteroalkylamino;

(b) optionally substituted heterocyclylalkyl;

(c) optionally substituted heterocyclylalkoxy;

(d) optionally substituted heterocyclylalkylamino;

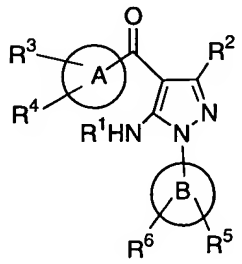
(e) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ - $NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl; or

(f) Z-alkylene-$NR^{30}R^{31}$ where Z is -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl, wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl); and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

APPENDIX B
PENDING CLAIMS

1. (Amended Herein) A compound selected from the group of compounds represented by Formula (I):



(I)

wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A and B are simultaneously an aryl or a heteroaryl ring;

R^3 is selected from the group consisting of:

(a) optionally substituted heterocyclyl;

(b) optionally substituted aryl or heteroaryl;

(c) heteroalkenyl;

(g) heteroalkynyl;

(e) optionally substituted heterocyclylalkyl;

(f) optionally substituted heterocyclylalkenyl;

(g) optionally substituted heterocyclylalkynyl;

(h) optionally substituted heterocyclylalkoxy, cyclyloxy or heterocyclyloxy;

(i) optionally substituted heterocyclylalkylamino;

(j) optionally substituted heterocyclylalkylcarbonyl;

(k) -Y-(alkylene)-R^9 where:

Y is a single bond, -O-, -NH- or -$S(O)_n$- (where n is an integer from 0 to 2); and

R^9 is cyano, optionally substituted heteroaryl, -COOH, -COR^{10}, -$COOR^{11}$, -$CONR^{12}R^{13}$, -SO_2R^{14}, -$SO_2NR^{15}R^{16}$, -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$, where R^{10} is optionally substituted heterocycle, R^{11} is alkyl, and R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(l) -$C(=NR^{20})(NR^{21}R^{22})$ where R^{20}, R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are -$(CH_2)_n$- where n is 2 or 3 and R^{22} is hydrogen or alkyl;

(m) -$NHC(X)NR^{23}R^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(n) -$CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

(o) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(p) arylaminoalkylene or heteroarylaminoalkylene;

(q) Z-alkylene-$NR^{30}R^{31}$ or Z-alkylene-OR^{32} where Z is -O-, and R^{30}, $R^{31}$and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl, wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl);

(r) -OC(O)-alkylene-CO_2H, -OC(O)-NR'R" , or CO_2NHR' (where R' and R" are independently hydrogen or alkyl);

(w) heteroarylalkenylene or heteroarylalkynylene; and

(x) heteroalkylamino;

R^4 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) alkoxy; and

(e) hydroxy;

R^5 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) haloalkyl;

(e) thioalkyl;

(f) hydroxy;

(g) amino;

(h) alkylamino;

(i) dialkylamino;

(j) heteroalkyl;

(k) optionally substituted heterocycle;

(l) optionally substituted heterocyclylalkyl;

(m) optionally substituted heterocyclylalkoxy;

(n) alkylsulfonyl;

(o) aminosulfonyl, mono-alkylaminosulfonyl or di-alkylaminosulfonyl;

(p) heteroalkoxy; and

(q) carboxy;

R^6 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl; and

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

2. (Amended Herein) The compound of Claim 1 wherein R^3 is:

(a) optionally substituted heterocyclyl;

(b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO_2R' (where R' is alkyl) or $SO_2NHR'R''$ (where R' and R" are independently hydrogen or alkyl);

(c) heteroalkenyl;

(d) heteroalkylamino;

(e) optionally substituted heterocyclylalkyl or heterocyclyloxy;

(f) optionally substituted heterocyclylalkenyl;

(g) optionally substituted heterocyclylalkynyl;

(h) optionally substituted heterocyclylalkoxy;

(i) optionally substituted heterocyclylalkylamino;

(j) optionally substituted heterocyclylalkylcarbonyl;

(o) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, $-CONR^{12}R^{13}$, SO_2R^{14}, $-SO_2NR^{15}R^{16}$ $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl,

(p) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(m) arylaminoalkylene or heteroarylaminoalkylene; or

(n) Z-alkylene-$NR^{30}R^{31}$ where Z is -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl, wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl).

3. The compound of Claim 2 wherein R^1 and R^2 are hydrogen; and B is phenyl.

4. The compound of Claim 3 wherein A is phenyl.

5. The compound of Claim 4 wherein R^4 is hydrogen; and R^5 is halo or alkyl.

6. The compound of Claim 5 wherein R^5 is chloro, fluoro or methyl; and R^6 is hydrogen, chloro, fluoro, methyl or methoxy.

7. The compound of Claim 5, wherein R^3 is optionally substituted heteroaryl.

8. The compound of Claim 7, wherein R^3 is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.

9. The compound of Claim 8, wherein R^3 is at the 3-position.

10. The compound of Claim 9, wherein R^5 is 4-F and R^6 is hydrogen.

11. The compound of Claim 9, wherein R^5 is 2-Me and R^6 is hydrogen.

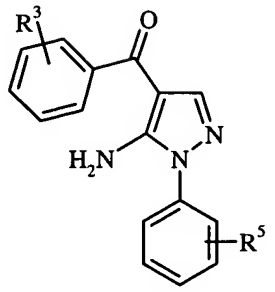
12. The compound of Claim 5, wherein R^3 is optionally substituted phenyl.

13. The compound of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

14. The compound of Claim 13, wherein R^3 is at the 3-position.

15. The compound of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.

16. (Amended Herein) A compound selected from the group of compounds represented by the Formula:



wherein:

R^5 is halo or alkyl; and

R^3 is:

(a) heteroalkylamino;

(b) optionally substituted heterocyclylalkyl;

(c) optionally substituted heterocyclylalkoxy;

(d) optionally substituted heterocyclylalkylamino;

(e) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ - $NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl; or

(f) Z-alkylene-$NR^{30}R^{31}$ where Z is -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl, wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl); and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

19. The compound of Claim 16, wherein R^5 is 2-F and R^6 is 4-F.

20. The compound of Claim 16, wherein R^5 is 4-F and R^6 is hydrogen.

21. The compound of Claim 16, wherein R^5 is 2-Me and R^6 is hydrogen.

22. The compound of Claim 16, wherein R^3 is heteroalkylamino.

23. The compound of Claim 22, wherein R^3 is at the 3-position and is selected from the group consisting of 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.

24. The compound of Claim 23 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

25. The compound of Claim 16, wherein R^3 is optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkoxy or optionally substituted heterocyclylalkylamino.

26. The compound of Claim 25, wherein R^3 is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl,4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxypiperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

27. The compound of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

28. The compound of Claim 16 wherein R^3 is -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.

29. The compound of Claim 28, wherein Y is a single bond and R^9 is SO_2R^{14} or -$SO_2NR^{15}R^{16}$.

30. The compound of Claim 29 wherein R^3 is methylsulfonylethyl or sulfamoylethyl.

31. The compound of Claim 30 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

32. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable excipient.

33. (New) The compound of Claim 1 wherein R^3 is selected from the group consisting of:

(a) optionally substituted heterocyclyl;

(b) optionally substituted aryl or heteroaryl, provided, however, that R^3 is not unsubstituted phenyl, unsubstituted thienyl, or unsubstituted pyrrolyl;

(c) heteroalkenyl;

(h) heteroalkynyl;

(e) optionally substituted heterocyclylalkyl;

(f) optionally substituted heterocyclylalkenyl;

(g) optionally substituted heterocyclylalkynyl;

(h) optionally substituted heterocyclylalkoxy, cyclyloxy or heterocyclyloxy;

(i) optionally substituted heterocyclylalkylamino;

(j) optionally substituted heterocyclylalkylcarbonyl;

(k) -Y-(alkylene)-R^9 where:

Y is a single bond, -O-, -NH- or -$S(O)_n$- (where n is an integer from 0 to 2); and

R^9 is cyano, optionally substituted heteroaryl, -COOH, -COR^{10}, -$COOR^{11}$, -$CONR^{12}R^{13}$, -SO_2R^{14}, -$SO_2NR^{15}R^{16}$, -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$, where R^{10} is optionally substituted heterocycle, R^{11} is alkyl, and R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or

heteroalkyl, provided, however, that -Y-(alkylene)-R^9 taken together are not $-(CH_2)_3-CO_2CH_3$ or $-CH_2-CO_2CH_2CH_3$;

(l) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20}, R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $-(CH_2)_n-$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;

(m) $-NHC(X)NR^{23}R^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(n) $-CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

(o) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(p) arylaminoalkylene or heteroarylaminoalkylene;

(q) Z-alkylene-$NR^{30}R^{31}$ or Z-alkylene-OR^{32} where Z is -O-, and R^{30}, $R^{31}$and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl, wherein said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl);

(r) -OC(O)-alkylene-CO_2H, -OC(O)-NR'R" , or CO_2NHR' (where R' and R" are independently hydrogen or alkyl);

(v) heteroarylalkenylene or heteroarylalkynylene;

(w) heteroalkylamino; and

(x) iodo.